

# Current and Prospective Utilization of Innovator Biologics and Biosimilars in Ontario

A Report by the Ontario Drug Policy Research Network



## About the ODPRN

The Ontario Drug Policy Research Network (ODPRN) is a province-wide network of researchers who provide timely, high quality, relevant drug policy research to decision makers. We conduct research to determine real-world drug utilization, safety, effectiveness, and costs of drugs in Ontario, and have developed partnerships that allow us to engage in cross-provincial comparisons of drug safety and utilization.

We are funded to conduct pharmacoepidemiologic and drug policy research as part of an initiative to provide evidence to inform policy at the Ontario Ministry of Health (MOH). As such, the ODPRN works closely with the Drugs and Devices Division (DDD) of the Ontario MOH and other stakeholders to select key priority areas and topics for analysis.

### How to cite this report:

Tadrous M, McCormack D, Martins D, Kitchen S, Singh S, Gomes T. *Current and Prospective Utilization of Innovator Biologics and Biosimilars in Ontario*. Toronto: Ontario Drug Policy Research Network; January 2020. DOI 10.31027/ODPRN.2020.01.

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## Acknowledgements

This study was supported by the ODPRN, which is funded by grants from the Ontario MOH. This study was also supported by ICES, which is funded by an annual grant from the Ontario MOH. Parts of this material are based on data and information compiled and provided by the Canadian Institute for Health Information (CIHI).

The opinions, results, and conclusions reported in this paper belong to the authors and are independent from the funding sources. No endorsement by ICES, CIHI, or the Ontario MOH is intended or should be inferred. We thank IMS Brogan Inc. for use of their Drug Information Database. All datasets used were linked using unique encoded identifiers and analyzed at ICES in Toronto, Ontario ([www.ices.on.ca](http://www.ices.on.ca)). The Canadian Agency for Drugs and Technologies in Health (CADTH) provided guidance on the study design to ensure relevance to Canadian decision-makers.

## Study Team

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# Executive Summary

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## Publicly-Funded Biologic Utilization in Ontario

- A total of \$1.1 billion was spent on biologic medications through the public drug program in Ontario in 2018, which represented a nearly 3-fold increase from \$352.9 million in 2010. Total annual costs are expected to reach \$1.4 billion by 2021 (95% CI: \$1.3 billion, \$1.5 billion).
- The total number of biologic users in Ontario has increased by 462.3% over the past 9 years, from 21,383 users (Q1-2010) to 120,247 users (Q2-2019). The number of users is projected to increase an additional 95.3% to 162,020 users by Q2-2022 (95% CI: 137,436, 186,455).
- Biosimilar users accounted for only 3.6% (N=4,300 of 120,247 users) of all biologic users in Ontario in the second quarter of 2019.
- The highest cost biologics in 2018 were aflibercept (\$290.0 million), ranibizumab (\$188.3 million), and infliximab (\$117.5 million), representing 27.9%, 17.4%, and 10.9% of total biologic spending, respectively.

## Utilization of Select Publicly-Funded Biologics Indicated for Rheumatic Conditions and Inflammatory Bowel Disease

- The quarterly number of publicly-funded biologic users for rheumatic conditions and inflammatory bowel disease (IBD) in Ontario increased by 133.1% over the past 9 years, from 5,225 users (Q1-2010) to 12,178 users (Q2-2019). The number of users is projected to increase an additional 40.4% to 14,287 users (95% CI: 13,550, 15,023) by Q2-2022.
- Among infliximab and etanercept, two biologics with a currently available biosimilar, only 16.7% of users (N=1,196 of 7,158) were treated with a biosimilar in Q2-2019. If these trends continue, it is estimated that 2,717 users (95% CI: 1,899, 3,536) of all infliximab and etanercept users (N=8,142; 95% CI: 7,438, 8,847) will be treated with biosimilars by Q2-2022, representing a proportion of 35.1% (95% CI: 24.5%, 45.6%).
- Following the introduction of biosimilars for rheumatic conditions and IBD, infliximab biosimilar users increased to 13.8% (N=539 of 3,905) of all infliximab users in Q2-2019. Similarly, etanercept biosimilar users increased to 20.2% (N=659 of 3,256) of all etanercept users by Q2-2019.
- The uptake of biosimilars was greater among users for rheumatic conditions, with etanercept and infliximab biosimilar users making up 20.2% (N=659 of 3,256) and 26.6% (N=203 of 764) of all etanercept and infliximab biologic users, respectively, by Q2 2019. In contrast, infliximab biosimilar users for IBD made up only 6.9% of all infliximab biologic users (N=187 of 2,712) by Q2-2019.

### Take-Away Messages

- Biosimilar users accounted for a small proportion of overall biologic users, even among biologics with a currently available biosimilar.
- Although etanercept was reimbursed through a Limited Use access program and infliximab was reimbursed through the Exceptional Access Program, there was similar uptake of their respective biosimilar products. This suggests that traditional formulary-based policies may not have a significant impact on biosimilar uptake.
- There was a greater uptake in biosimilars among patients with rheumatic conditions relative to patients with IBD. This suggests that the effect of policies on the uptake of biosimilars may differ by patient indication.

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# Background

Biologic drugs are large complex biological compounds derived from living organisms that have become important treatment options across a wide number of medical conditions, including rheumatic conditions, gastrointestinal disease, and diabetes.<sup>1</sup> The use of biologics has had a measurable impact on patient outcomes, often in diseases with little to no treatment options. Yet, biologics have substantially higher prices than other less complex, chemically-derived pharmaceuticals, and their growth in use threatens the sustainability of public drug programs. Importantly, not only do biologics have higher prices, but they also are prescribed for longer durations to younger patients in order to manage chronic diseases. These expanding costs continue to put pressure on public payers, who struggle to curb drug costs as the fastest growing healthcare expenditure in the Canadian health care system.<sup>2</sup> In 2018, 3 of the top 5 most costly medications in Canada were biologics.<sup>3</sup>

A biosimilar biologic drug, or biosimilar, is a drug that is highly similar and has no clinically meaningful differences compared to an innovator biologic drug that has already been authorized for sale.<sup>1</sup> Biosimilars can be used for the same therapeutic aim and offer an opportunity to reduce spending on costly innovator biologics.<sup>1</sup> Unfortunately, biosimilars appear to be underutilized due to a multitude of factors at the policy-level (e.g. regulatory requirements) and at the consumer-level (e.g. patient and physician preferences).<sup>4</sup> As a result, public payers in Canada have begun developing policies designed to increase the use of biosimilar drugs. These approaches generally focus on transitioning eligible patients from innovator biologics to a lower cost biosimilar, for specific clinical conditions. Essential to this work is a better understanding of the current use of biologics and biosimilars across various clinical conditions.

This report aims to describe the current utilization patterns and expenditures of innovator biologics and biosimilars through the public drug program in Ontario, Canada.

## Objectives

1. Examine the current utilization and expenditures of innovator biologics and biosimilars indicated for rheumatic conditions and inflammatory bowel disease (IBD).
2. Forecast the utilization and expenditures of innovator biologics and biosimilars indicated for rheumatic conditions and IBD.
3. Explore differences in the uptake of biosimilars by patient medical conditions (i.e. rheumatic conditions and IBD) and by drug type (e.g. etanercept and infliximab).

## Methods

### Setting and Cohort Definition

We conducted a cross-sectional study among individuals living in Ontario, Canada who were dispensed a publicly-funded innovator biologic or biosimilar through the Ontario Drug Benefit (ODB) program between January 1, 2010 and June 30, 2019. A list of these medications can be found in **Appendix Table 3**. Low molecular weight heparins and insulin products were excluded to allow for easier interpretability of the results as they are simpler biologic products with more common use and a longer history of use. In Ontario, individuals are eligible for the ODB program if they are unemployed, receiving support for disability or home care services, have high prescription drug costs relative to net household income, reside in a long-term care facility, or are aged 65 years or older. In January 2018, Ontario introduced OHIP+ to provide public drug coverage to individuals under the age of 25. This program was modified

on April 1, 2019 to limit coverage to those without private drug insurance. To account for the changes in OHIP+ during our study period, we excluded prescription claims for individuals who became newly eligible for public drug coverage through OHIP+ between January 1, 2018 and April 1, 2019. To do this, we excluded individuals who received a biologic or biosimilar drug between January 1, 2018 and April 1, 2019, and who did not receive these medications between January 2016 and December 2017. Individuals who received prescriptions through the modified OHIP+ program between April 1, 2019 and June 30, 2019 were included in the analysis, since drug utilization during this revised OHIP+ program is likely to continue moving forward.

## Data Sources

### Ontario Drug Benefit Database

The ODB database was used to extract individual-level prescription claims data for all biologic and biosimilar prescriptions dispensed to Ontario residents eligible for public drug funding. Eligibility criteria included unemployment, disability, high prescription drug costs relative to net household income, receipt of home care services, residence in a long-term care facility, or age 65 years or older. Between January 2018 and March 2019, the program also covered individuals aged 24 years or younger, and from April 1, 2019 onwards, eligibility included individuals aged 24 years or younger without private drug insurance. This database is of high quality, with an error rate of <1% and can be linked to other health administrative databases to obtain patient demographic information.<sup>5</sup>

### Patient Medical Conditions

We used the validated ICES Ontario Crohn's and Colitis Cohort (OCCC) database<sup>6</sup> to determine past diagnoses of IBD (crohn's and ulcerative colitis). To determine past diagnoses of rheumatic

conditions (rheumatic arthritis, psoriasis, and psoriatic arthritis), the Ontario Rheumatoid Arthritis Database<sup>7</sup> (ORAD) and the Ontario Psoriasis and Psoriatic Arthritis datasets<sup>8</sup> were used. The OCCC database has specific methods and sensitivity based on the patient's age group, with sensitivity ranging from 59.3% to 91.1% and specificity ranging from 96.2% to 99.5%. ORAD is limited to individuals over the age of 15 and has a sensitivity of 78% and a specificity of 100%. The Psoriasis and Psoriatic Arthritis database has a specificity of 99% and 100% and a sensitivity of 52% and 51% for psoriasis and psoriatic arthritis, respectively. All databases use hospital and physician visits to identify past diagnoses and only include cases up to March 31, 2018. Therefore, individuals with a new diagnosis of rheumatic conditions or IBD between April 1, 2018 and June 30, 2019 were not captured and were placed into an unknown diagnosis group. We anticipate the unknown group will largely be comprised of individuals who were not captured by the validated cohorts because of the relatively low sensitivity of these databases and limitations of when these databases were last updated. A small number of individuals may be using biologic treatments for less common off-label conditions, such as ankylosing spondylitis or other off-label uses and would also be captured in the unknown group.<sup>9</sup>

### Other Health Administrative Databases

We used data from the Ontario Registered Persons Database (RPDB), Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) and National Ambulatory Care Reporting System (CIHI-NACRS) database, Ontario Health Insurance Plan (OHIP) database, and the ICES Physician Database (IPDB).



# Measures of Interest

## Trends in Innovator Biologic and Biosimilar Utilization

We report quarterly trends in the utilization of publicly-funded biologics in Ontario between January 1, 2010 (Q1-2010) and June 30, 2019 (Q2-2019), overall and stratified by the type of biologic (i.e. innovator biologic or biosimilar). Utilization was defined as the number of individuals who were dispensed a prescription for a publicly-funded biologic or biosimilar per quarter. We also report utilization restricted to a subset of biologic tumor necrosis inhibitor antagonists indicated for rheumatic conditions and IBD (**Table 1**). This subset is of interest to policy-makers in Canada, either because they have marketed biosimilars (infliximab, etanercept), or because a biosimilar is pending commercialization (adalimumab) in which case the innovator can be used as a “negative control”

in this analysis. We stratified this analysis by drug type (i.e. infliximab, adalimumab, etanercept) and by patient indication (i.e. rheumatic conditions [rheumatoid arthritis, psoriatic arthritis and psoriasis] or IBD). Particularly, individuals who received more than one biologic drug type or who had both IBD and a rheumatic condition in a given time period are counted in each subgroup.

## Trends in Expenditures for Biologics

We report quarterly trends in expenditures of publicly-funded biologics in Ontario, between January 1, 2010 (Q1-2010) and June 30, 2019 (Q2-2019). Here, we defined total costs as the price of a drug including mark-up fees, dispensing fees, and deductibles fees. We also conducted sensitivity analyses excluding these fees and found no significant changes to our results.

**Table 1. Innovator biologics and biosimilars for rheumatic conditions and IBD included in this report**

Medication (Generic Name)	Brand Name	Medical Indication <sup>a</sup>	Type of Biologic	Earliest Dispensing Date from the ODB	ODB Formulary Listing Date	Current Listing <sup>b</sup>
<b>Infliximab</b>	Remicade	RC & IBD	Innovator	Jan 29, 2002	---	Exceptional Access Program
	Inflectra	RC & IBD	Biosimilar	Feb 26, 2016	Feb 25, 2016	Limited Use
	Renflexis	RC & IBD	Biosimilar	Sept 27, 2018	Sept 27, 2018	Limited Use
<b>Adalimumab</b>	Humira	RC & IBD	Innovator	Jun 10, 2005	Sept 9, 2010	Limited Use
<b>Etanercept</b>	Enbrel	RC	Innovator	May 2, 2001	Dec 3, 2008	Limited Use
	Brenzys	RC	Biosimilar	Aug 2, 2017	Jul 31, 2017	Limited Use
	Erelzi	RC	Biosimilar	Jan 15, 2018	Dec 21, 2017	Limited Use

a. IBD=Inflammatory Bowel Disease (i.e. crohn's and ulcerative colitis), RC= Rheumatic Conditions (i.e. rheumatic arthritis, psoriasis, and psoriatic arthritis).

b. The Exceptional Access Program facilitates patient access to drugs not funded on the ODB Formulary, where no listed alternative is available, and requires prior authorization. Limited Use products require special clinical criteria/conditions to be met in order to be reimbursed under the ODB program, but are generally available without a requirement of prior authorization.<sup>10</sup>

# Forecasting

Trends in utilization and expenditures for biologics were forecasted between July 1, 2019 and June 30, 2022 using quarterly trends from the previous nine years (January 1, 2010 to June 30, 2019). We used Holt-Winters' exponential smoothing models to forecast utilization and costs. Either the additive or multiplicative method was used to

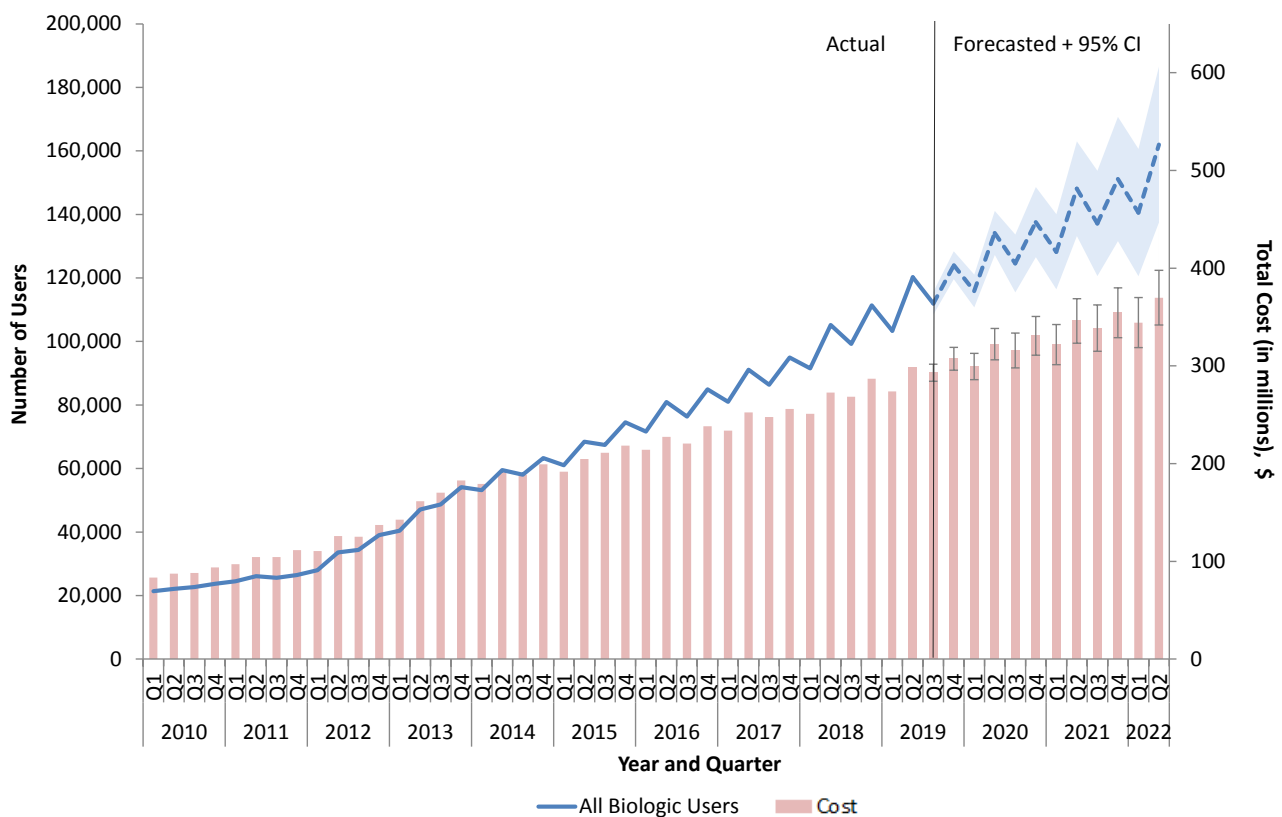
achieve optimal model fit accounting for seasonal variation.

All databases used in this study were linked using unique, encoded identifiers, and analyzed at ICES using SAS Enterprise Guide Version 7.1. Use of these data was authorized under section 45 of Ontario's Personal Health Information Protection Act (PHIPA), which does not require review by a research ethics board.

## Key Findings

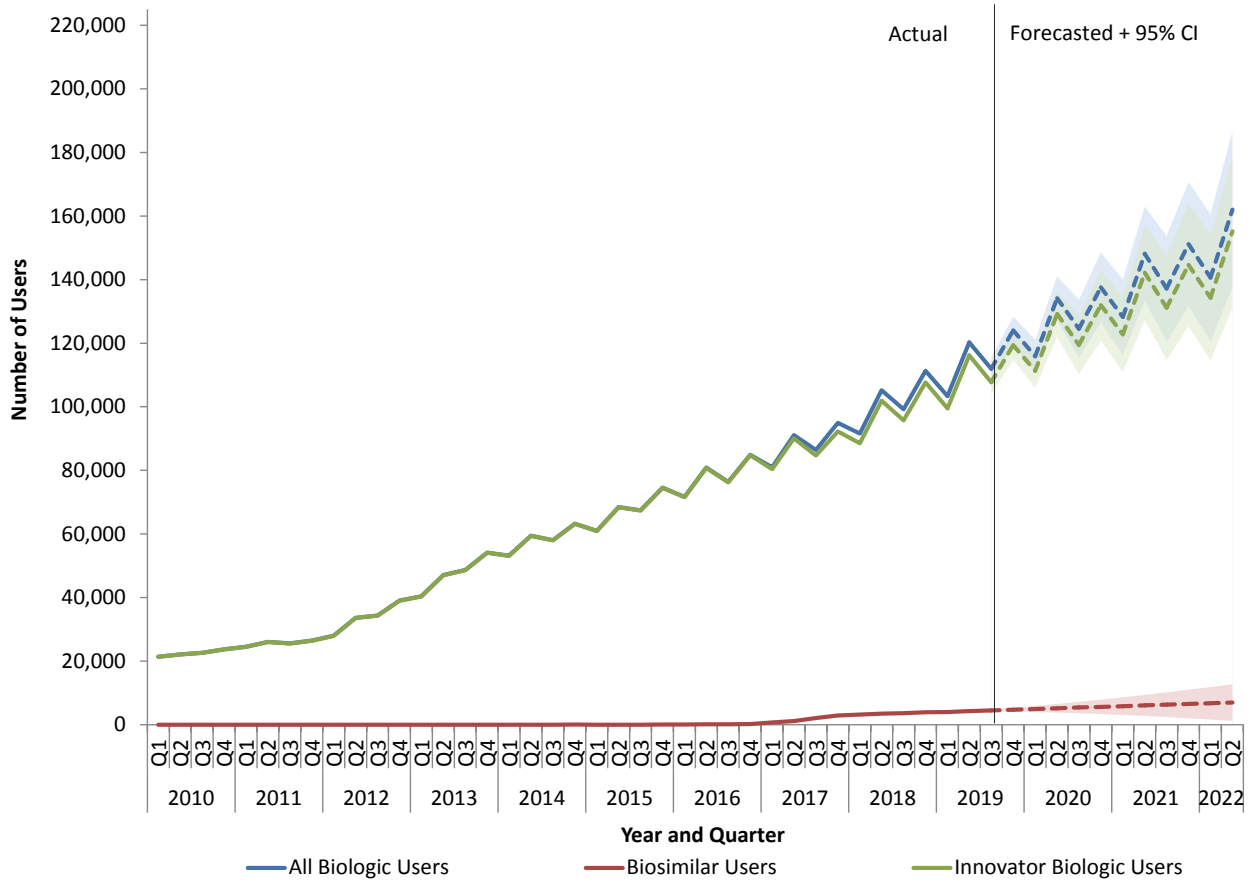
### Trends in Utilization and Costs of All Available Innovator Biologics and Biosimilars in Ontario between 2010 and 2022

**Figure 1. Utilization and expenditures of all biologics between 2010 and 2022**



The number of biologic users has increased by 462.3% from the first quarter of 2010 (N=21,383) to the second quarter of 2019 (N=120,247). Costs similarly increased by 257.5% during the same period (from \$83.5 million to \$298.6 million). The quarterly number of users and costs are projected to increase to 162,020 users (95% CI: 137,436, 186,455) and \$369.8 million (95% CI: \$341.9 million, \$397.8 million) by Q2-2022.

Figure 2. Utilization of all biologics between 2010 and 2022



Biosimilar users accounted for 3.6% (N=4,300 of 120,247) of all biologic users and 4.7% of costs (\$14.0 million of \$298.6 million) in the second quarter of 2019. By Q2-2022, the number of biosimilar users (6,995 users [95% CI: 1,234, 12,756]) is projected to represent 3.4% (95% CI: 0%, 11.0%) of all biologic users (162,020 users [95% CI: 137,486, 186,553]).

**Table 2. Highest cost biologics in calendar year 2018**

Rank	Drug Name	Users	Prescriptions Dispensed	Total Annual Cost (%) <sup>b</sup>	Total Cost per User
1	Aflibercept	30,481	161,872	\$290,003,049 (26.9)	\$9,514
2	Ranibizumab	20,181	97,497	\$188,280,607 (17.4)	\$9,330
3	Infliximab <sup>a</sup>	4,314	26,946	\$117,536,231 (10.9)	\$27,245
4	Adalimumab	5,545	40,005	\$90,468,148 (8.4)	\$16,315
5	Denosumab	101,337	174,088	\$72,788,757 (6.7)	\$718
6	Etanercept <sup>a</sup>	3,841	27,709	\$61,729,962 (5.7)	\$16,071
<b>Overall</b>		183,900	552,866	\$1,078,992,733	\$5,867

a. Has a currently available biosimilar.

b. Total costs were defined as the price of a drug, including mark-up, dispensing fees, and deductibles.

The biologic with the highest total cost was aflibercept, which accounted for \$290 million in spending in 2018. Biologics used for rheumatic conditions and IBD included infliximab, adalimumab, and etanercept. These were ranked as the 3rd, 4th, and 6th highest cost biologics in 2018, respectively.

### Summary of Findings for Figure 1, Figure 2, and Table 1

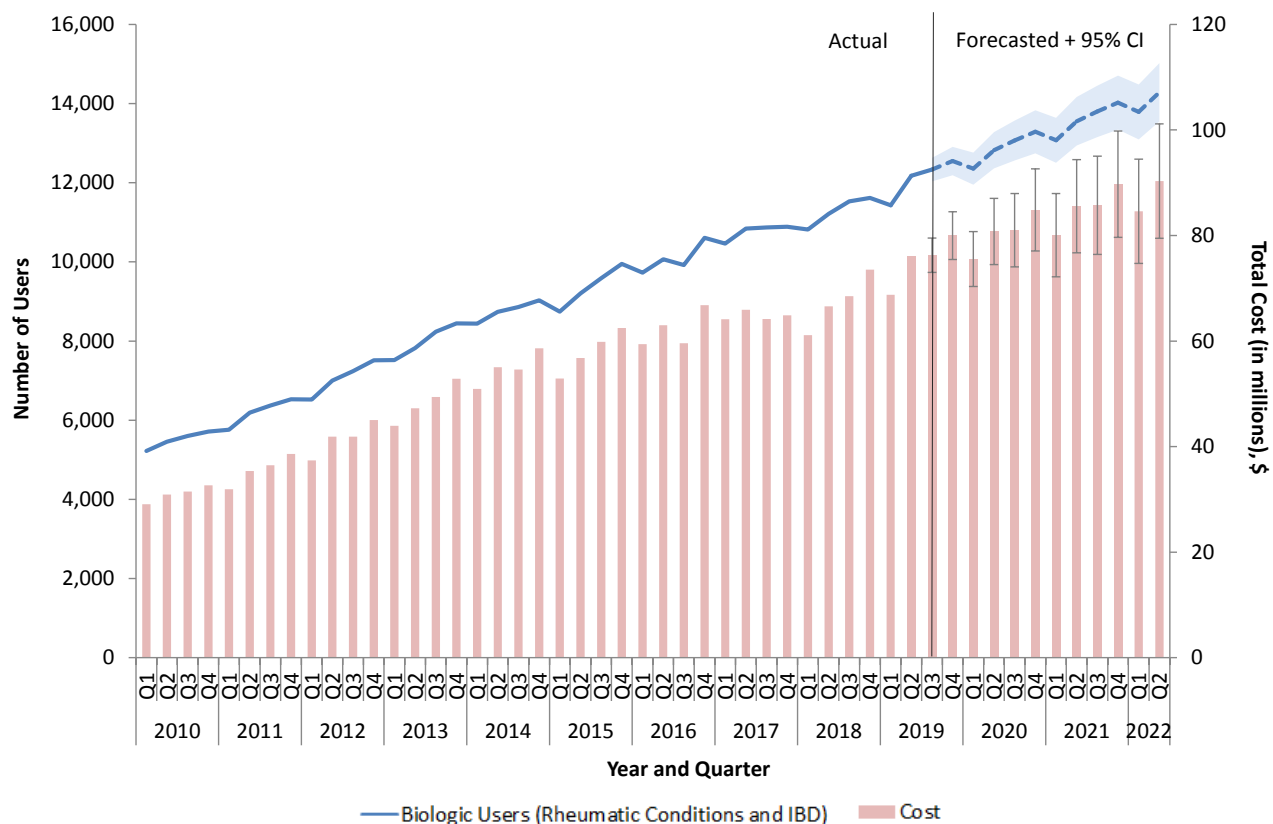
- The number of publicly-funded biologic users in Ontario has increased by 462.3% over the past 9 years, from 21,383 users (Q1-2010) to 120,247 users (Q2-2019). The number of users is projected to increase an additional 95.3% to 162,020 users (95% CI: 137,486, 186,553) by Q2-2022 (**Figure 1**).
- Biosimilar users accounted for 3.6% (N=4,300 of 120,247) of all biologic users in Ontario in the second quarter of 2019. By Q2-2022, the number of biosimilar users (6,995 users (95% CI: 1,234, 12,756) is projected to represent 3.4% (95% CI: 0%, 11.0%) of all biologic users (162,020 users [95% CI: 137,486, 186,553]) (**Figure 2**).
- A total of \$1.1 billion was spent annually on all publicly-funded biologic medications in Ontario in 2018. This represented an increase of 205.7% from 2010 (\$352.9 million annually). Total costs are expected to increase to \$1.4 billion annually by 2021 (95% CI: \$1.3 billion, \$1.5 billion) (**Figure 1**).
- The highest cost biologics in 2018 were aflibercept (\$290.0 million), ranibizumab (\$188.3 million), and infliximab (\$117.5 million) (**Table 2**).

# Trends in Utilization and Costs of Innovator Biologics and Associated Biosimilars for Rheumatic Conditions and IBD from 2010 to 2022

## Methodological Note:

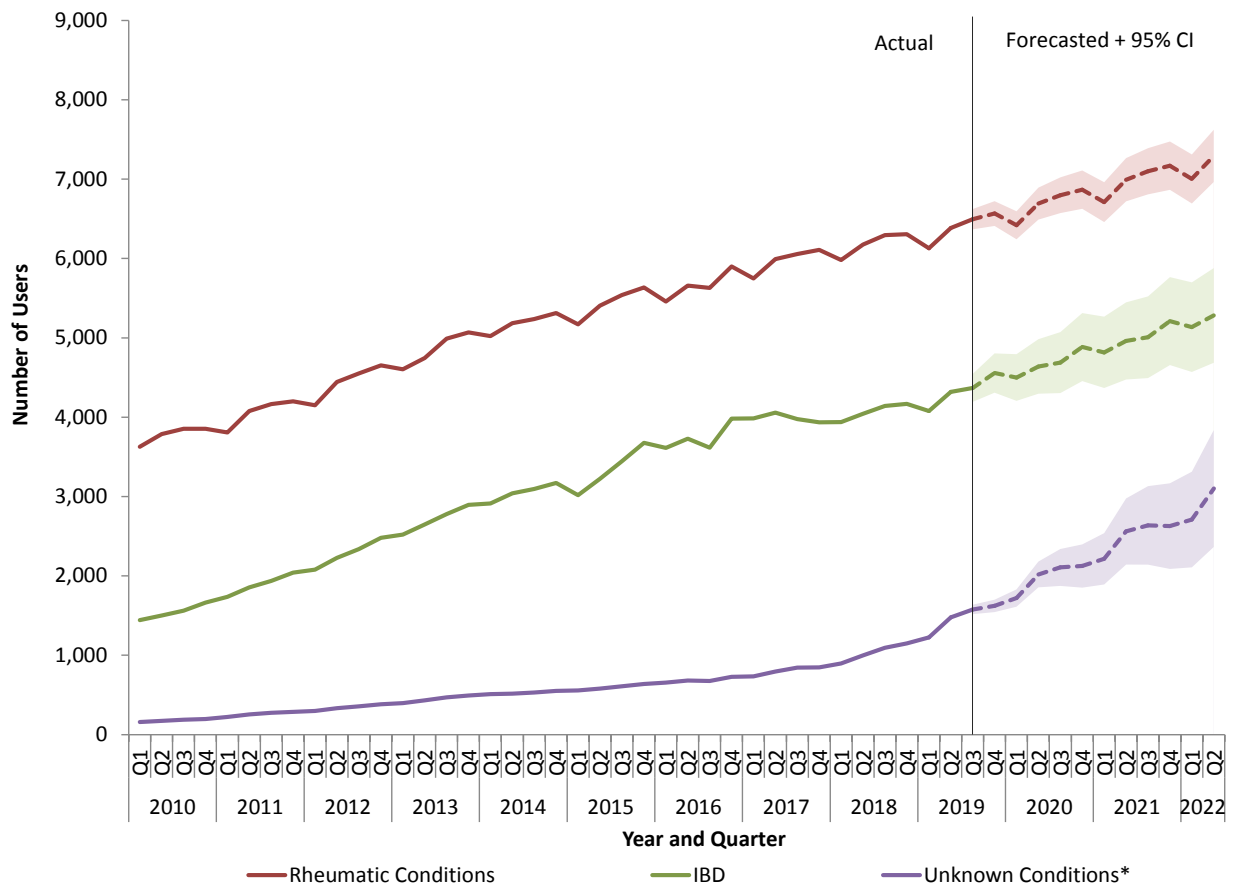
We defined biologics for rheumatic conditions and IBD as infliximab, adalimumab, and etanercept. Infliximab and etanercept currently have biosimilars available (**Table 1**). These biologics make up 10.1% of all biologic users in Ontario (N=12,178 of 120,247), and their associated biosimilars make up 27.8% of all biosimilar users in Ontario (N=1,196 of 4,300).

**Figure 3. Utilization and expenditures of biologics indicated for rheumatic conditions and IBD between 2010 and 2022**



The utilization of biologics indicated for rheumatic conditions and IBD increased by 133.1% from the first quarter of 2010 (N=5,225) to the second quarter of 2019 (N=12,178). Quarterly costs similarly increased 161.5% during that same period, from \$29.1 million to \$76.1 million. The number of biologic users for rheumatic conditions and IBD is projected to increase an additional 40.4% by the second quarter of Q2-2022, reaching 14,287 users (95% CI: 13,550, 15,023).

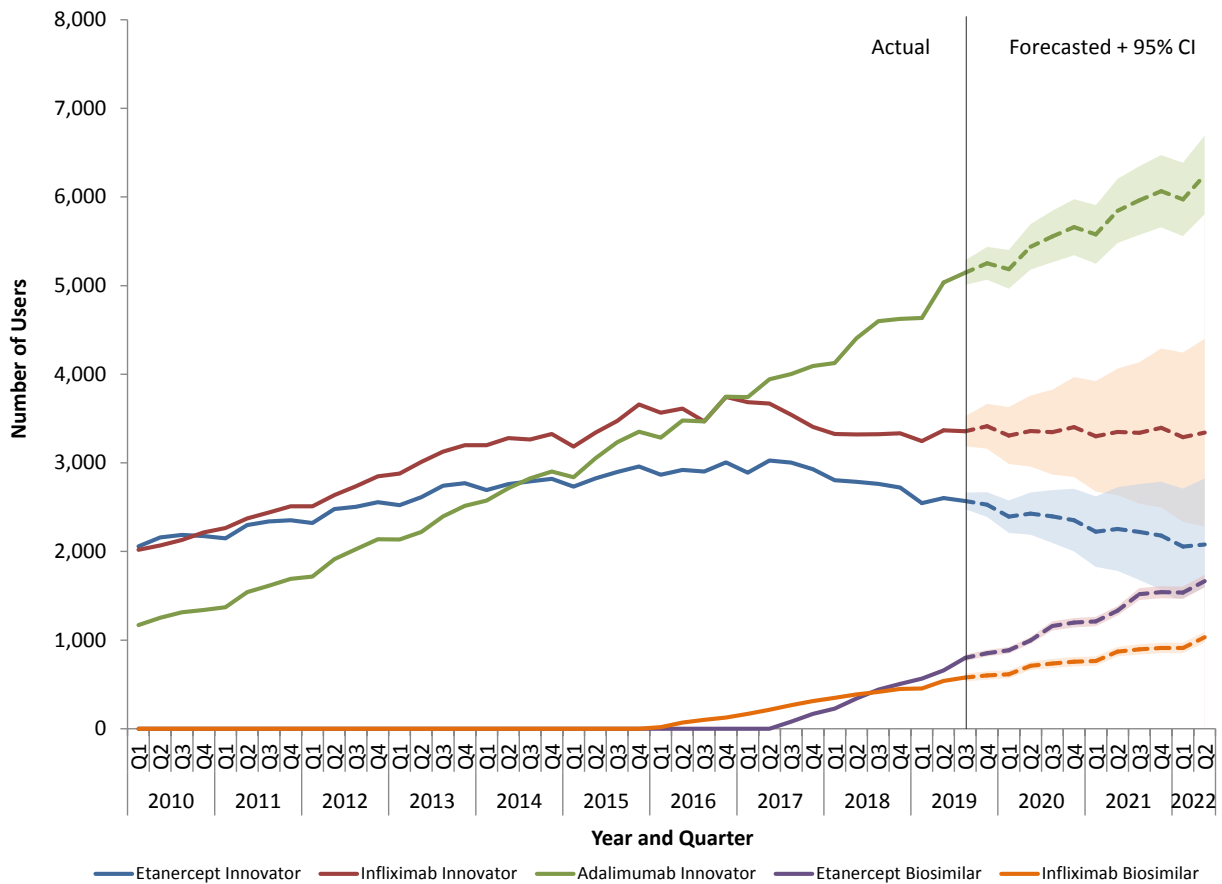
**Figure 4. Utilization of biologics for rheumatic conditions and IBD by indication between 2010 and 2022**



\*The rise in users for unknown conditions following Q2-2018 corresponds with the last update of the validated rheumatic conditions and gastrointestinal databases, which included diagnosed cases up to March 31, 2018. Therefore, the proportion of unknown conditions may be overestimated in this figure.

Among biologics users receiving medications for rheumatic conditions and IBD, about half (52.4%) used biologics for rheumatic conditions, followed by 35.5% for IBD, and 12.1% for unknown indications in Q2-2019. The breakdown of biologics for rheumatic conditions and IBD is projected to remain relatively constant to Q2-2022.

**Figure 5. Utilization of biologics for rheumatic conditions and IBD by drug type between 2010 and 2022<sup>a</sup>**



<sup>a</sup>The number of users by drug type includes users for unknown conditions.

Among biologics indicated for rheumatic conditions and IBD with a currently available biosimilar (infliximab and etanercept), 16.7% of users (N=1,196 of 7,158) were treated with a biosimilar in Q2-2019. By Q2-2022, it is estimated that biosimilar users will make up 35.1% (95% CI: 24.5%, 45.6%) of selected biologic users with a currently available biosimilar. Generally, the use of biologics for rheumatic conditions and IBD was increasing from Q1-2010 to Q2-2016. However, in correspondence with the introduction of their first available biosimilars, infliximab and etanercept innovator biologic users decreased by 6.8% (from 3,613 users in Q2-2016 to 3,368 users in Q2-2019) and 13.3% (from 3,003 users in Q3-2017 to 2,603 users in Q2-2019), respectively.

## Summary of Findings for Publicly-Funded Biologics Indicated for Rheumatic Conditions and IBD: Figure 3, Figure 4, and Figure 5

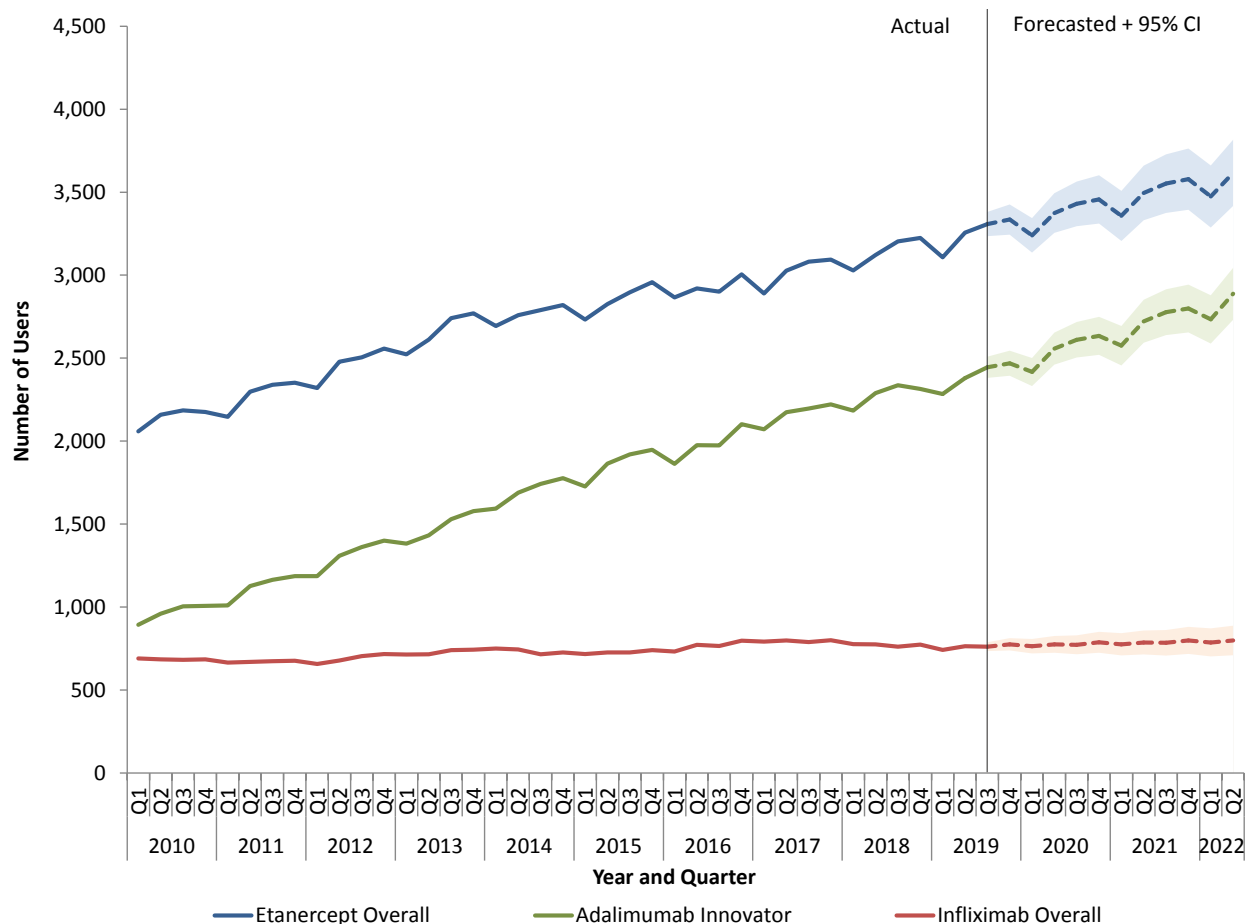
- Quarterly biologic utilization indicated for rheumatic conditions and IBD (adalimumab, etanercept, and infliximab) made up 10.1% of all biologic users in Ontario in Q2-2019 (N=12,178 of 120,247). The use of these biologics has increased by 133.1% over the past 9 years, from 5,225 users in Q1-2010 to 12,178 users in Q2-2019, and are projected to increase an additional 40.4% (14,287 users; 95% CI: 13,550, 15,023) by Q2-2022 (**Figure 3**).
- The total annual cost of biologics indicated for rheumatic conditions and IBD (infliximab, etanercept, and adalimumab) reached \$269.7 million annually in Ontario in 2018. Annual costs are projected to increase an additional 57.0% to \$340.6 million (95% CI: \$304.6 million, \$376.6 million) in 2021 (**Figure 3**).
- Among biologics indicated for rheumatic conditions and IBD, about half of users (52.4%; N=6,385) used these for rheumatic conditions and 35.5% (N=4,318) for IBD in Q2-2019. The indication for use could not be determined for 12.1% (N=1,477) of individuals in Q2-2019. Some individuals may be misclassified in the unknown group following March 30, 2018, which was the last date available to identify patient indication (**Figure 4**).
- Among biologics indicated for rheumatic conditions and IBD with a currently available biosimilar (infliximab and etanercept), 16.7% of users (N=1,196 of 7,158) were treated with a biosimilar in Q2-2019. By Q2-2022, it is estimated that 2,717 users (95% CI: 1,899, 3,536) out of 8,142 biologic users (95% CI: 7,438, 8,847) with a currently available biosimilar will be treated with biosimilars, representing a proportion of 35.1% (95% CI: 24.5%, 45.6%) (**Figure 5**).
- Increases in utilization of innovator biologics indicated for rheumatic conditions and IBD between Q3-2017 and Q2-2019 were largely driven by increases in adalimumab use (25.8% increase; from 4,003 to 5,036 users) (**Figure 5**).
- Following the introduction of their first available biosimilars, the number of infliximab and etanercept innovator biologic users decreased by 6.8% (from 3,613 users in Q2-2016 to 3,368 users in Q2-2019) and 13.3% (from 3,003 users in Q3-2017 to 2,603 users in Q2-2019), respectively (**Figure 5**).
- Infliximab biosimilar users for rheumatic conditions and IBD increased from 1.9% of all infliximab users in Q2-2016 (N=70 of 3,682) to 13.8% in Q2-2019 (N=539 of 3,905). Etanercept biosimilar users increased from 2.6% of all etanercept users for rheumatic conditions and IBD in Q3-2017 (N=80 of 3,081) to 20.2% in Q2-2019 (N=659 of 3,256) (**Figure 5**).



# Trends in Utilization and Costs of Innovator Biologics and Associated Biosimilars for Rheumatic Conditions and IBD by Indication from 2010 to 2022

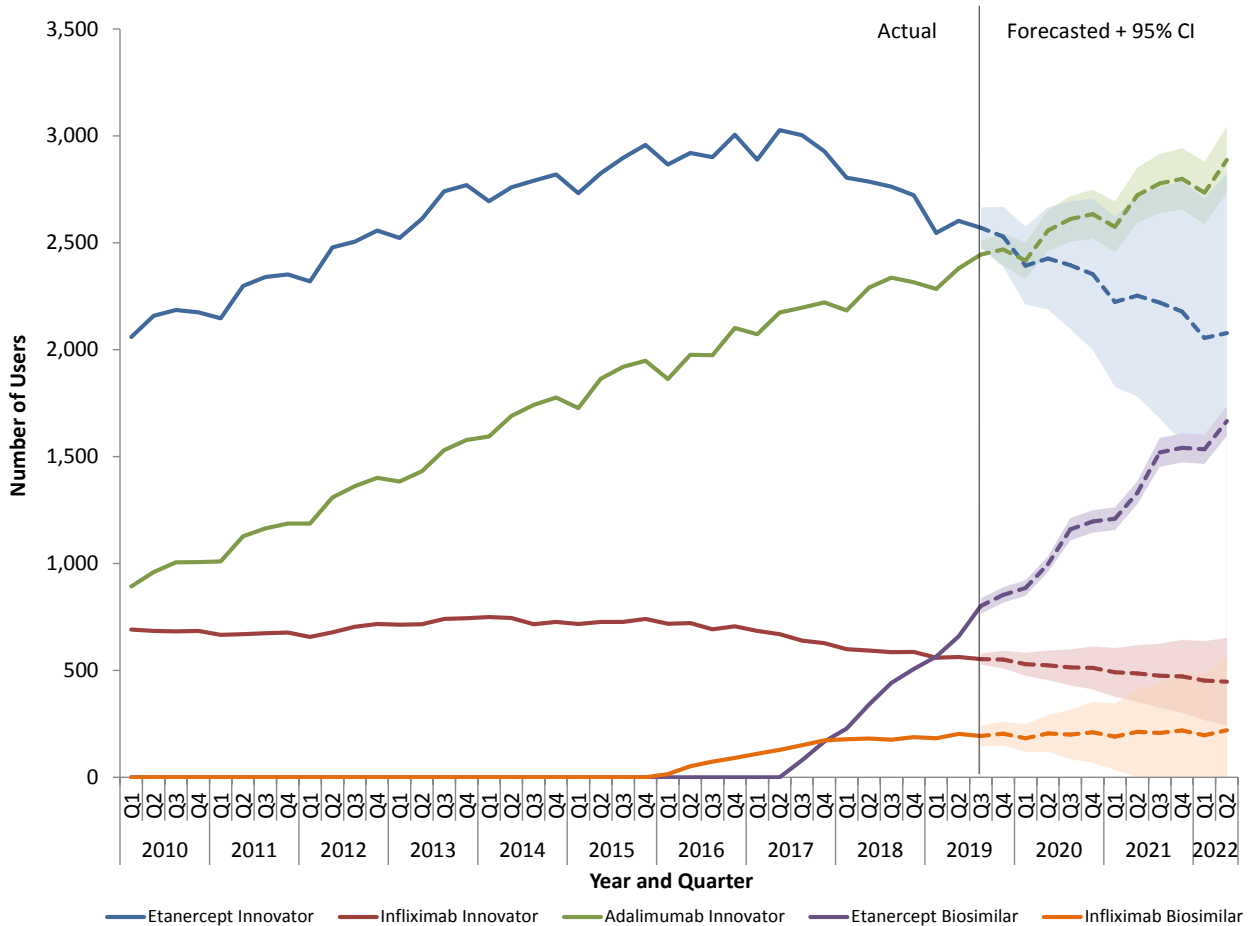
## BIOLOGICS INDICATED FOR RHEUMATIC CONDITIONS

Figure 6. Utilization of biologics indicated for rheumatic conditions between 2010 and 2022



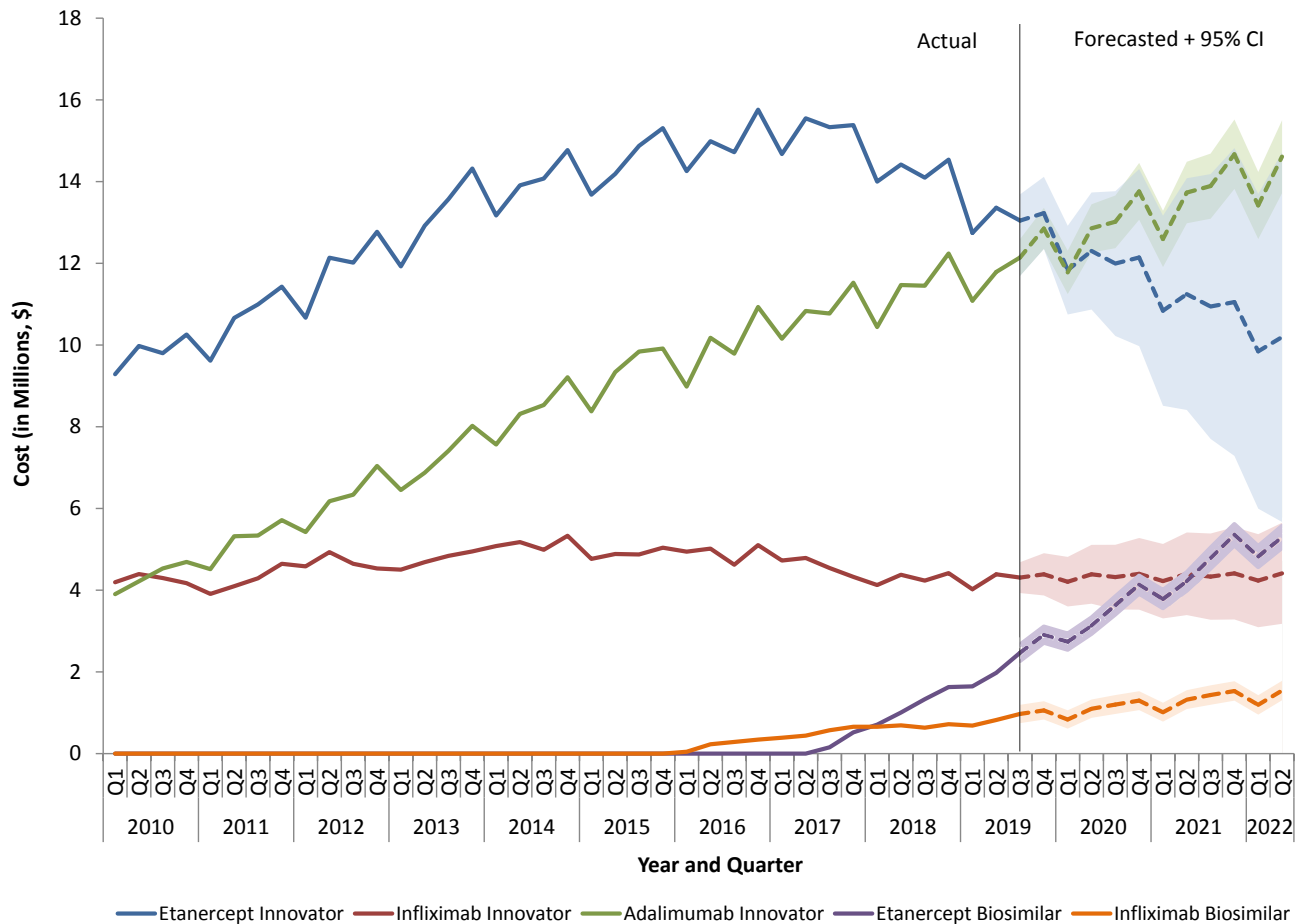
From 2010 to 2019, adalimumab innovator users for rheumatic conditions increased by the largest amount (166.5%; from 893 users in Q1-2010 to 2,380 users in Q2-2019). Overall, etanercept and infliximab users (innovator and biosimilar biologics) for rheumatic conditions increased by 58.1% and 10.6% during the same time period, respectively.

**Figure 7. Utilization of innovator and biosimilar biologics indicated for rheumatic conditions between 2010 and 2022**



Etanercept and infliximab biosimilar users made up 20.2% (N=659 of 3,256) and 26.6% (N=203 of 764) of all etanercept and infliximab biologic users for rheumatic conditions in Q2-2019. If current trends continue, by Q2-2022, etanercept and infliximab biosimilar users are projected to reach 51.3% (95% CI: 48.3%, 54.2%) and 30.3% (95% CI: 0%, 70.7%) of all etanercept and infliximab biologic users for rheumatic conditions, respectively.

**Figure 8. Total costs of innovator and biosimilar biologics indicated for rheumatic conditions by drug type between 2010 and 2022**



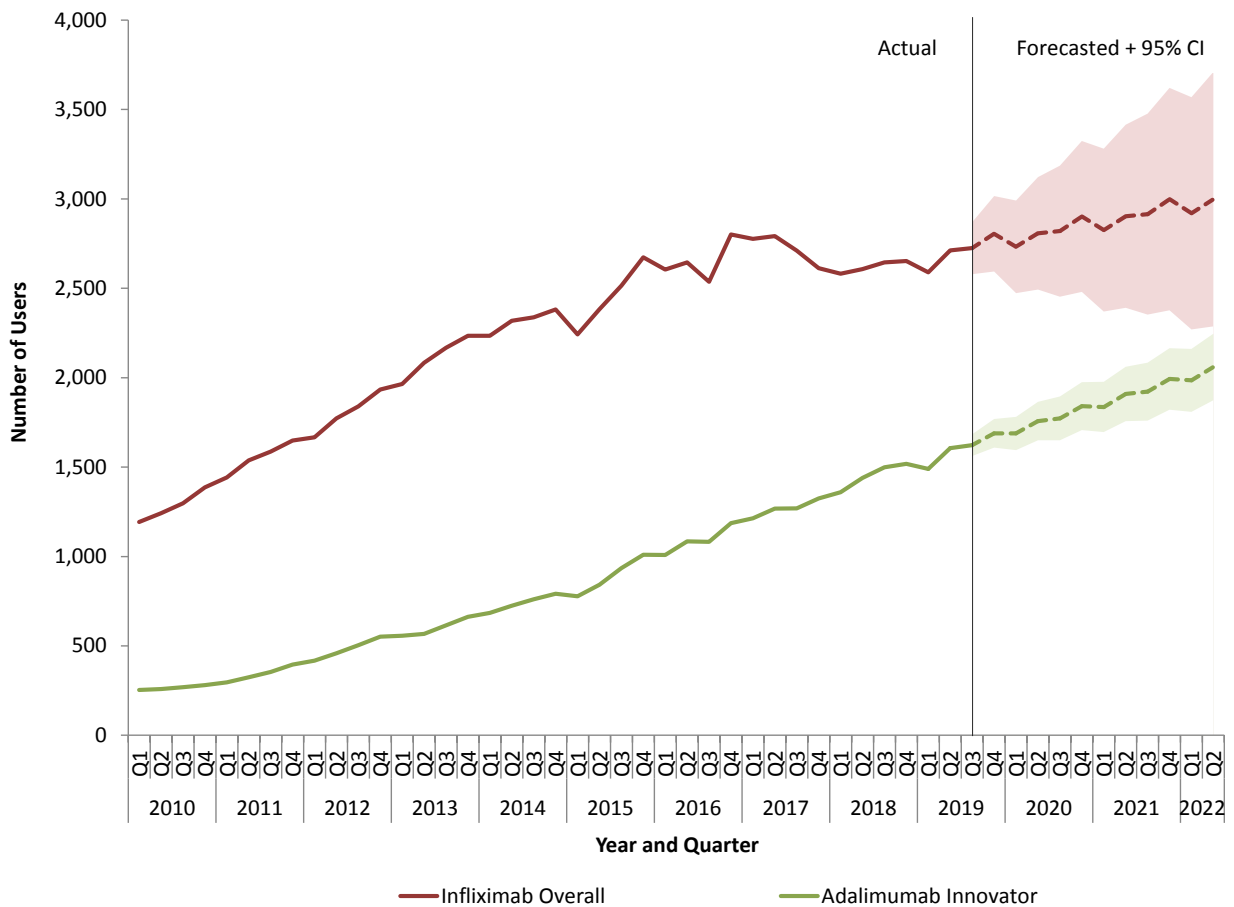
Etanercept and infliximab biosimilar costs made up 12.9% (\$2.0 million of \$15.3 million) and 15.8% (\$822,263 of \$5.2 million) of total etanercept and infliximab costs for rheumatic conditions, respectively, in Ontario in Q2-2019. By Q2-2022, etanercept and infliximab biosimilar costs are expected to make up 34.5% (95% CI: 32.7%, 36.3%) and 30.5% (95% CI: 25.3%, 35.7%) of total etanercept and infliximab costs, respectively. The fastest growing cost over the study period was for adalimumab, which increased by 202.6%, from \$3.9 million in Q1-2010 to \$11.8 million in Q2-2019.

## Summary of Findings for Selected Publicly-Funded Biologics Indicated for Rheumatic Conditions: **Figure 6, Figure 7, and Figure 8**

- From 2010 to 2019, adalimumab innovator users for rheumatic conditions increased by 166.5% from 893 users in Q1-2010 to 2,380 users in Q2-2019. Overall etanercept and infliximab users (innovator and biosimilar biologics) for rheumatic conditions increased by 58.1% and 10.6% during the same time period, respectively (**Figure 6**).
- Etanercept and infliximab biosimilar users made up 20.2% (N=659 of 3,256) and 26.6% (N=203 of 764) of all etanercept and infliximab biologic users for rheumatic conditions, respectively, in Q2-2019. If current trends continue, by Q2-2022, etanercept biosimilar users (1,666; 95% CI: 1,596, 1,736) and infliximab biosimilar users (220; 95% CI: 0, 569) are projected to reach 51.3% (95% CI: 48.3%, 54.2%) and 30.3% (95% CI: 0%, 70.7%) of all etanercept biologic users (3,616; 95% CI: 3,417, 3,816) and infliximab biologic users (799; 95% CI: 710, 888) for rheumatic conditions, respectively (**Figure 7**).
- Following the introduction of Brenzys, an etanercept biosimilar, in Q3-2017, and a second biosimilar, Erelzi in Q1-2018, etanercept biosimilar users increased from 2.6% of all etanercept users for rheumatic conditions (N=80 of 3,081) in Q3-2017 to 20.2% (N=659 of 3,256) in Q2-2019 (**Figure 7**).
- Following the introduction of two infliximab biosimilars, Inflectra in Q1-2016 and Renflexis in Q3-2018, infliximab biosimilar users for rheumatic conditions increased from 6.7% of all infliximab biologic users for rheumatic conditions (N=52 of 733) in Q2-2016 to 26.6% (N=203 of 764) in Q2-2019 (**Figure 7**).
- Etanercept and infliximab biosimilar costs for rheumatic conditions made up 12.9% (\$2.0 million of \$15.3 million) and 15.8% (\$822,263 of \$5.2 million) of total etanercept and infliximab costs for rheumatic conditions in Ontario in Q2-2019. By Q2-2022, etanercept biosimilar costs (\$5.3 million; 95% CI: \$5.0 million, \$5.6 million) are expected to make up 34.5% (95% CI: 32.7%, 36.3%) of total etanercept biologic costs for rheumatic conditions (\$14.8 million; 95% CI: \$11.8 million, \$17.8 million). Infliximab biosimilar costs (\$1.5 million; 95% CI: \$1.3 million, \$1.8 million) are expected to make up 30.5% (95% CI: 25.3%, 35.7%) of total infliximab biologic costs (\$5.5 million; 95% CI: \$4.4 million, \$6.6 million) for rheumatic conditions in Q2-2022. (**Figure 8**).
- Following the introduction of etanercept biosimilars, the cost of etanercept innovator biologics for rheumatic conditions decreased by 13.1% from \$15.3 million in Q3-2017 to \$13.3 million in Q2-2019 (**Figure 8**).
- Similarly, following the introduction of infliximab biosimilars, the cost of infliximab innovator biologics for rheumatic conditions decreased by 12.0% from \$5.0 million in Q2-2016 to \$4.4 million in Q2-2019 (**Figure 8**).
- The fastest growing cost over the study period was for adalimumab, which increased by 202.6%, from \$3.9 million in Q1-2010 to \$11.8 million in Q2-2019 (**Figure 8**).

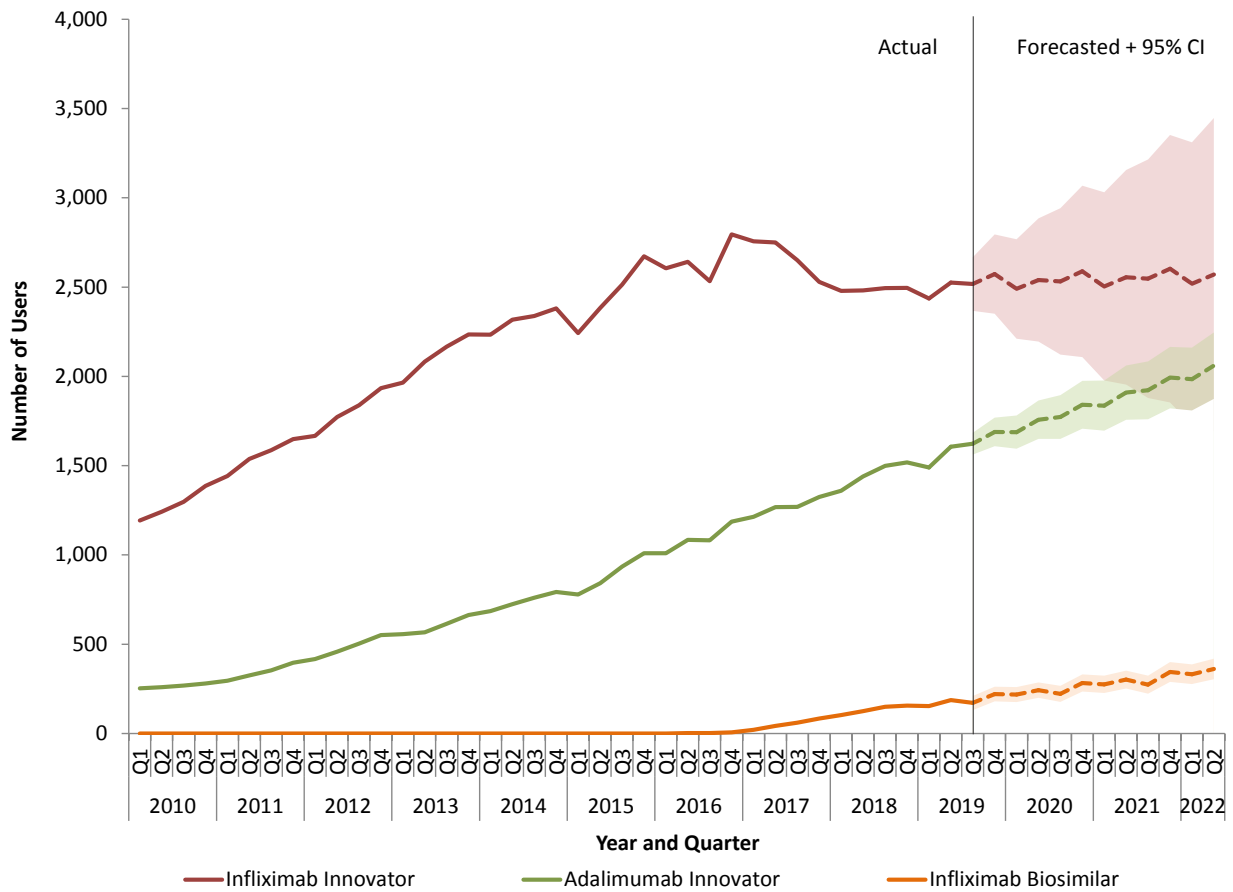
# BIOLOGICS INDICATED FOR INFLAMMATORY BOWEL DISEASE

Figure 9. Utilization of biologics indicated for IBD between 2010 and 2022



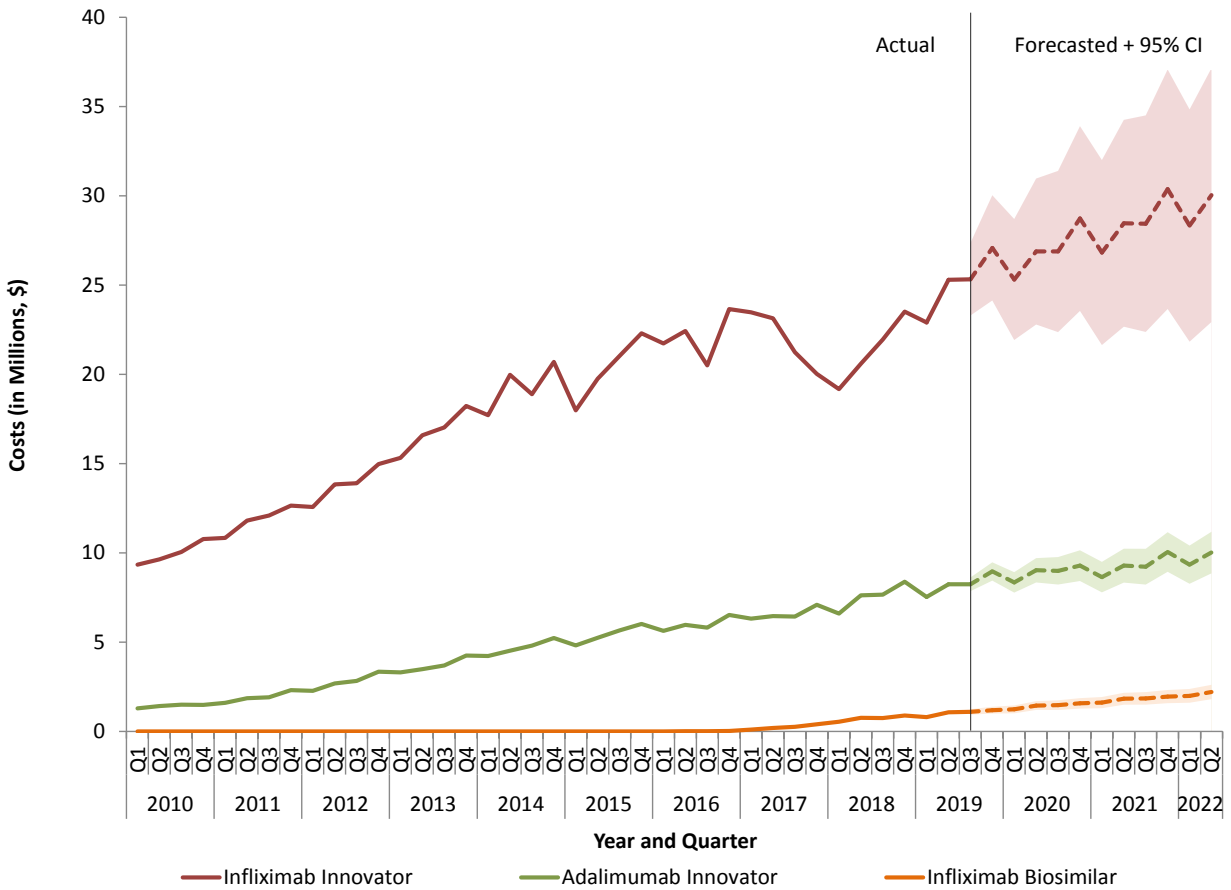
Overall, infiximab users (innovator and biosimilar biologics) for IBD increased by 127.3% from 1,193 users in Q1-2010 to 2,712 users in Q2-2019. Adalimumab innovator biologic users for IBD increased by 534.5% from 253 users in Q1-2010 to 1,606 users in Q2-2019.

**Figure 10. Utilization of innovator and biosimilar biologics indicated for IBD between 2010 and 2022**



Infiximab biosimilar users (N=187) made up only 6.9% of all infiximab biologic users for IBD (N=2,712) in Q2-2019. If current trends continue, by Q2-2022, infiximab biosimilar users (N=362; 95% CI: 304, 419) are projected to make up 13.1% (95% CI: 10.8%, 15.3%) of infiximab biologic users for IBD (N=2,999; 95% CI: 2,287, 3,710).

**Figure 11. Total costs of innovator and biosimilar biologics indicated for IBD between 2010 and 2022**



Note: The dip in costs from Q1-2018 to Q2-2019 may be a consequence of a limitation for this analysis that involved excluding new biologic users from the OHIP+ program as detailed in the methods section.

In Q2-2019, infliximab biosimilar costs (\$1.1 million) made up 4.1% of total infliximab costs (\$26.4 million) for IBD in Ontario. By Q2-2022, infliximab biosimilar costs are expected to make up 8.7% (95% CI: 7.3%, 10.0%) of all infliximab costs for IBD. The cost of adalimumab for IBD increased steadily by 530.7% from \$1.3 million in Q1-2010 to \$8.2 million in Q2-2019.

## Summary of Findings for Publicly-Funded Biologics Indicated for IBD: Figure 9, Figure 10, and Figure 11

- Overall, infliximab users for IBD increased by 127.3% from 1,193 users in Q1-2010 to 2,712 users in Q2-2019. Adalimumab innovator users for IBD increased by 534.5% from 253 users in Q1-2010 to 1,606 users in Q2-2019 (**Figure 9**).
- In Q2-2019, infliximab biosimilar users (N=187) made up only 6.9% of all infliximab biologic users for IBD (N=2,712). If current trends continue, by Q2-2022, infliximab biosimilar users (N=362; 95% CI: 304, 419) are projected to make up 13.1% (95% CI: 10.8%, 15.3%) of infliximab biologic users for IBD (N=2,999; 95% CI: 2,287, 3,710) (**Figure 10**).
- Following the introduction of two infliximab biosimilars, Inflectra in Q1-2016 and Renflexis in Q3-2018, infliximab biosimilar users for IBD increased from 0.1% of all infliximab biologic users for IBD (N=3 of 2,645) in Q2-2016 to 6.9% (N=187 of 2,712) in Q2-2019. During this same time period, infliximab innovator users decreased by 4.4% (from 2,642 users to 2,525 users) and adalimumab innovator users increased by 48.0% (from 1,085 users to 1,606 users) (**Figure 10**).
- The cost of infliximab biosimilars for IBD accounted for 0.04% of total infliximab biologic costs for IBD in Q2-2016 (\$8,939 of \$22.4 million) and 4.1% (\$1.1 million of \$26.4 million) in Q2-2019. By Q2-2022, infliximab biosimilar costs (\$2.2 million; 95% CI: \$1.8 million, \$2.6 million) are expected to make up 8.7% (95% CI: 7.3%, 10.0%) of all infliximab biologic costs for IBD (\$31.3 million; 95% CI: \$24.4 million, \$25.4 million). The cost of adalimumab for IBD increased steadily by 530.7% from \$1.3 million in Q1-2010 to \$8.2 million in Q2-2019. Etanercept is not indicated for IBD (**Figure 11**).
- After the introduction of infliximab biosimilars, the cost of infliximab innovator biologics for IBD increased by 12.9% from \$22.4 million in Q2-2016 to \$25.3 million in Q2-2019 (**Figure 11**).
- Whereas infliximab biosimilar users made up 26.5% of all infliximab biologic users for rheumatic conditions (N=203 of 764), infliximab biosimilar users made up only 6.9% of all infliximab biologic users for IBD (N=187 of 2,712) in Q2-2019 (**Figure 7, Figure 10**).

## Discussion

There has been consistent and significant growth in the number of publicly-funded individuals receiving biologic treatments in Ontario and the associated costs to the government between 2010 and 2019. This growth is expected to continue, with costs estimated to reach \$1.4 billion annually in 2021. More recently, the use of biosimilars has grown, but still only comprises a small proportion of total biologic users for products where a

biosimilar option is available. This was especially true among biologics indicated for IBD, possibly due to a greater concern within the IBD community around the use of biosimilars.<sup>11</sup> Importantly, the uptake of biosimilars among rheumatic conditions appears to have curbed growth in spending for these products despite the continuously increasing number of users. In contrast, costs continued to increase for adalimumab, which does not currently have a biosimilar option. These findings highlight the potential for biosimilars



to limit and to potentially reduce the financial burden of biologic spending on the public-payer.

Notably, although the policy of biologics for etanercept and infliximab differed, with Enbrel (an etanercept innovator) listed as a Limited Use product as of July 2017 compared to Remicade (an infliximab innovator) listed under the Exceptional Access Program as of January 2014, the relative uptake of biosimilars for these two drug classes did not differ significantly.<sup>12,13</sup> This may suggest that traditional formulary-based policies may not be effective at significantly altering biosimilar uptake.

A possible reason for this differing response in uptake, following a policy change influencing biologics relative to other pharmaceutical products, could be associated with the irregularly high cost of biologics. The higher cost and complexity of use has led to a strong integration of patient support programs, which may be encouraging innovator products over biosimilars through the use of patient assistance and cost-sharing programs.<sup>14,15</sup> Both patients and providers have commented that the existing infrastructure for innovator biologics, including the availability of infusion centers and patient support programs, may make these products more accessible to patients relative to biosimilars.<sup>11</sup> Therefore, new policy strategies specific to biologics, including evaluating the accessibility of similar patient supports for biosimilar products, may be required in order for policy-makers to observe meaningful increases in biosimilar use.

We would expect the patterns observed in this study to shift greatly with the development of new listing strategies. Since rheumatic conditions and IBD are chronic conditions, the potential impact would be greatest with a strategy that mandates non-medical controlled switching from a biologic to a biosimilar for all current users, and initiating a biosimilar for all new users, similar to the recent policies adopted in British Columbia.<sup>16</sup> A middle-

ground policy mandating biosimilar use for new users for rheumatic conditions and IBD would likely increase use of biosimilars, but would take longer to realize the full potential of cost savings associated with biosimilar uptake.

This study is not without limitations and the results of this analysis must be interpreted in the context of the design and the data used. First, diagnoses of comorbidities relied on administrative databases. Although many of these databases have been validated, and have reasonable sensitivity and specificity, some misclassification of diagnoses is possible. Secondly, the information on drug pricing is based on the claims submitted by pharmacies to the Ontario government. This information does not account for actual pricing paid by the government based on confidential listing agreements with manufacturers, and thus some of the cost may be overestimated. Lastly, the launch of OHIP+ coverage between January 2018 and March 2019 impacted future projections of biologic use and costs. As this policy was changed and did not reflect future public-payer costs, we excluded new OHIP+ beneficiaries between January 2018 to March 2019 from the analysis. Therefore, the true costs to the ODB program were underestimated during this time.

## Conclusion

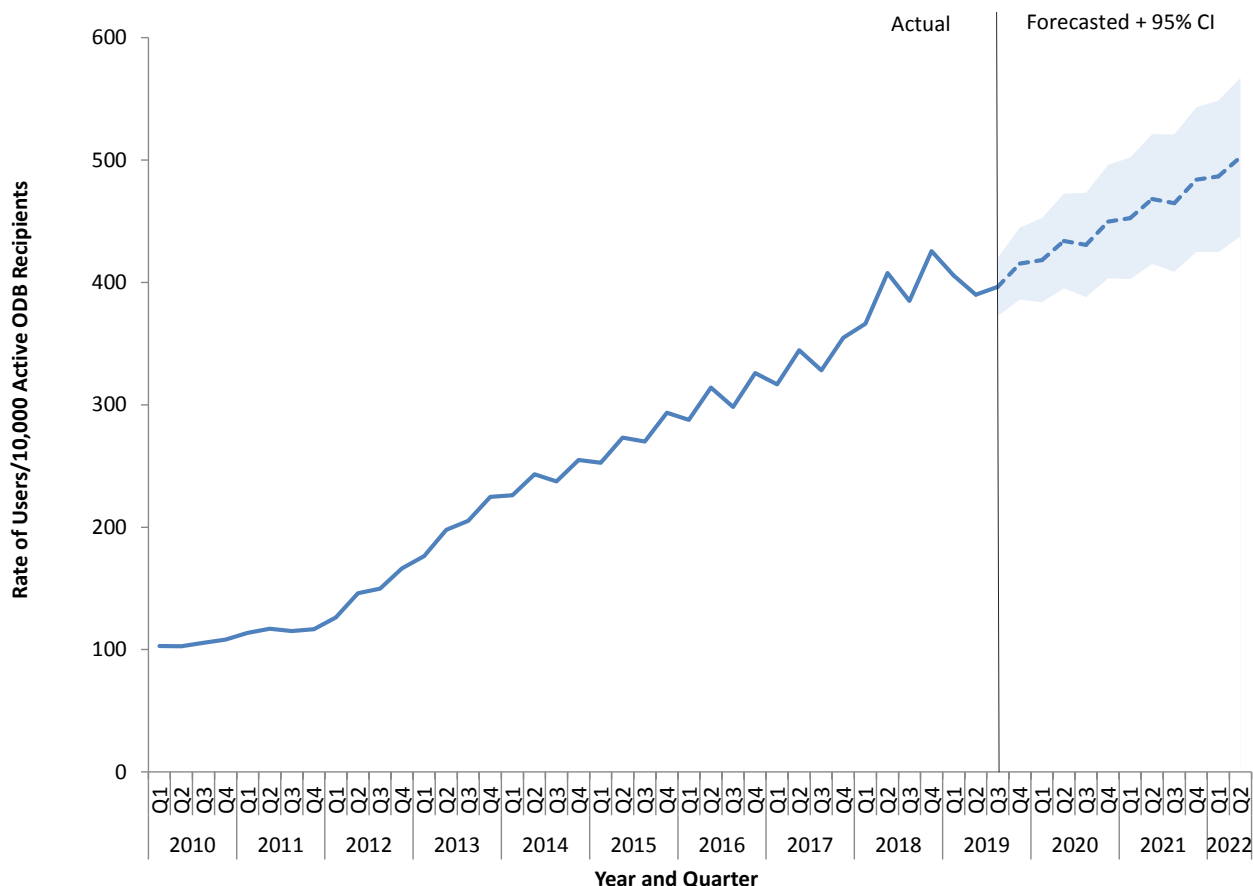
Utilization and public spending on biologic drugs continue to grow in Ontario, with a projected annual spending of nearly \$1.4 billion in 2021. In contrast, uptake of biosimilars has been low, with less than 1 in 5 biologic users accessing these less costly medications when they are available. Initiatives should be explored that could increase the utilization of biosimilars, given the large potential for cost savings for the government. These discussions should occur in consultation with people who use these medications and their prescribers to better understand the perspectives of those who would be affected by changes to these medications.

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# Appendix

**Figure A1. Rate of biologic users per 10,000 active ODB recipients between 2010 and 2022**



The rate of biologic users increased by 279% from 103 users to 390 users per 10,000 active ODB recipients between Q1-2010 and Q2-2019, and is projected to reach 502 users per 10,000 active ODB recipients (95% CI: 438, 567) by Q2-2022.

**Table A1. List of innovator biologics and biosimilars included in the report**

Abatacept	Canakinumab	Erythropoietin	Infliximab	Omalizumab	Rituximab
Adalimumab	Certolizumab	Etanercept	Interferon Alfa 2B	Peginterferon Alfa 2A	Romiplostim
Adenosine	Darbepoetin	Filgrastim	Interferon Alfa 2B & Ribavirin	Peginterferon Alfa 2A & Ribavirin	Somatrem
Aflibercept	Denosumab	Glatiramer	Interferon Beta	Peginterferon Alfa-2B & Ribavirin	Somatropin
Alemtuzumab	Eculizumab	Glucagon	Interferon Beta-1B	Pegvisomant	Tocilizumab
Anakinra	Elosulfase	Golimumab	Natalizumab	Porfimer	Ustekinumab
Bevacizumab	Epoetin	Idursulfase	Ocriplasmin	Ranibizumab	